#24 9

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of
Ibrahim, et al.

Group Art Unit: 1655

Serial No.: 09/444,095

Examiner: Sisson, B.

Filed: November 22, 1999

FOR: Purification Method and Apparatus

* * * * *

AMENDMENT

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Sir:

Responsive to the Office Action dated April 1, 2002, please enter the following amendments and consider the following remarks.

IN THE CLAIMS:

Please amend the claims as follows:

31. (Thrice Amended) A method of DNA or RNA purification comprising:

placing a DNA or RNA containing sample in a first reservoir tube with a solution to effect release of DNA or RNA from cells in said sample;

inserting a wand into said first reservoir tube, wherein said wand comprises a cap, a sample collection assembly and an elongated shaft connecting said cap to said sample collection assembly, said sample collection assembly having microstructures for increasing the surface area of the sample collection assembly;

securely and sealingly closing said first reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said first reservoir tube;

agitating said first reservoir tube to mix said sample with said solution under conditions for releasing said DNA or RNA from cells in said sample and non-specifically

binding said DNA or RNA to said microstructures of said sample collection assembly, thereby non-specifically binding said DNA or said RNA to said microstructures of said sample collection assembly;

removing said wand from said first reservoir tube and inserting said wand into a second reservoir tube, said second reservoir tube containing a wash buffer;

securely and sealingly closing said second reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said second reservoir tube;

agitating said second reservoir tube to mix said sample with said wash buffer under conditions to retain only said DNA or said RNA on said microstructures;

removing said wand from said second reservoir tube and inserting said wand into a third reservoir tube, said third reservoir tube containing an elution buffer, wherein said elution buffer causes release of said nucleic acids from said microstructures;

incubating said third reservoir tube; and

recovering purified DNA or RNA from said third reservoir tube.

32. (Amended) The method of claim 31, wherein said sample capture assembly comprises a main body having one or more flanges with microstructures for binding target molecules.

33. (Amended) The method of claim 32, wherein said microstructures are selected from the group consisting of cross-etched lanes, dimples, pillars and pores.

34. (Amended) The method of claim 31, wherein said microstructures are selected from the group consisting of cross-etched lanes, dimples, pillars and pores.

35 (Amended) The method of claim 31, wherein said sample collection assembly comprises a mesh outer surface wherein said microstructures are microparticles enclosed within said mesh outer surface.

G3

38. (Amended) The method of claim 31, wherein said microstructures of said sample collection assembly are coated with a material that binds non-specifically with nucleic acids.

G4

63. (Amended) A method of purifying specific DNA or RNA comprising:

placing a purified DNA or RNA sample in a first reservoir tube under conditions to denature double stranded DNA or render RNA suitable for binding;

inserting a wand into said first reservoir tube, wherein said wand comprises a cap, a sample collection assembly and an elongated shaft connecting said cap to said sample collection assembly, said sample collection assembly having microstructures for increasing the surface area of the sample collection assembly, and said microstructures of said sample collection assembly are coated with a coating comprising sequence specific oligonucleotide probe, peptide nucleic acid probe through a linker arm, or biotin-streptavidin bond to capture specific target DNA or RNA;

securely and sealingly closing said first reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said first reservoir tube, and incubating said DNA or said RNA of the sample in the sample collection assembly under conditions whereby stable, specific hybridization structures are formed, thereby binding said specific DNA or said specific RNA to said coating on said microstructures of said sample collection assembly;

removing said wand from said first reservoir tube and inserting said wand into a second reservoir tube, said second reservoir tube containing a wash buffer;

securely and sealingly closing said second reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said second reservoir tube;

agitating said second reservoir tube to mix said sample with said wash buffer under conditions to retain only said DNA or said RNA on said microstructures;

removing said wand from said second reservoir tube and inserting said wand into a third reservoir tube, said third reservoir tube containing an alkaline elution buffer to effect release of said DNA or said RNA;

incubating said third reservoir tube;

removing said sample collection assembly from said third reservoir tube;

adding neutralization buffer to said third reservoir tube to stabilize said DNA or said RNA; and

recovering said specific DNA or RNA from said third reservoir tube.

Please cancel claim 64.

Please add claims 68 through 70 as follows:

68. (New) The method of claim 64, wherein said DNA coating is single stranded DNA and double stranded hybridization structures are formed.

69. (New) The method of claim 64, wherein said DNA coating is double stranded DNA and triplex hybridization structures are formed.

70. (New) A method of purifying specific DNA or RNA comprising:

placing a purified DNA or RNA sample in a first reservoir tube under conditions to denature double stranded DNA or render RNA suitable for binding;

inserting a wand into said first reservoir tube, wherein said wand comprises a cap, a sample collection assembly and an elongated shaft connecting said cap to said sample collection assembly, said sample collection assembly having microstructures for increasing the surface area of the sample collection assembly, and said microstructures of said sample collection assembly are coated with a coating comprising sequence specific oligonucleotide probe, peptide nucleic acid probe through a linker arm, or biotin-streptavidin bond to capture specific target DNA or RNA;

securely and sealingly closing said first reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said first reservoir tube, and incubating said DNA or said RNA of the sample in the sample collection assembly under conditions whereby stable, specific hybridization structures are formed, thereby binding

said specific DNA or said specific RNA to said coating on said microstructures of said sample collection assembly;

removing said wand from said first reservoir tube and inserting said wand into a second reservoir tube, said second reservoir tube containing a wash buffer;

63 Cont.

securely and sealingly closing said second reservoir tube with said cap of said wand with said shaft and said sample collection assembly inside said second reservoir tube;

agitating said second reservoir tube to mix said sample with said wash buffer under conditions to retain only said DNA or said RNA on said microstructures;

removing said wand from said second reservoir tube and inserting said wand into a third reservoir tube;

heating said third reservoir tube under conditions to effect release of said DNA or said RNA from said microstructures;

removing said sample collection assembly from said third reservoir tube; and

recovering said specific DNA or RNA from said third reservoir tube.

REMARKS

Claims 31-35, 38, 39 and 63, and 65-70 are pending in the application. Claims 31-35, 38 and 63 have been amended. Claim 64 has been cancelled and the subject matter thereof has been inserted into claim 63. Claims 68-70 are newly added. No new matter has been added.

Claims 31-35, 38, 39 and 63-67 have been rejected under 35 U.S.C.§112, first paragraph as allegedly not enabled. Applicant respectfully traverses this rejection.

Pursuant to the discussions in the interview with the Examiner on June 25, 2002 and the Interview Summary dated June 25, 2002, Applicant's have made extensive amendments to the claims to address the Examiner's comments in the outstanding Office Action.

Applicants have addressed the issues of hybridization and amplification by these amendments. Further, amplification and hybridization are not the immediate subject matter of these claims as recited in the claimed steps.

Regarding the issue of deep reactive ion etching, Applicants state that this is a term of art and submit a declaration with exhibits indicating that this term was known at the time of the invention.

It is respectfully submitted that the present claims are in compliance with section 112, first paragraph and this rejection is overcome.

Claims 31-35, 38, 39 and 63-67 are rejected under 35 U.S.S. 103(a) as being unpatentable over Ji et al., in view of Henco et al., Piasio et al., Lockhart et al., Tuunanen (WO 94/18564). Applicant respectfully traverses this rejection.

The Examiner has combined two references that show the use of wands to increase surface area. The first reference showing a wand is Piasio et al.

Piasio et al. describes a method and apparatus for conducting a chemical reaction, primarily of antigen-antibody nature. There is no disclosure of binding nucleic acids. The apparatus in Piasio et al. is described at column 11 to have smooth surfaces to permit rapid draining of the reaction mixture when the matrix is removed from the solution. It further states that the material is plastic and has molded surfaces that are "polished, to a mirror smoothness." This feature actually teaches away from the present invention, which incorporates microstructures in its surfaces to maximize surface area.

The other reference that was cited to show the use of a wand to increase surface area is Tuunanen. Tuunanen is directed to an immunoassay. There is no discussion of how to capture or purify nucleic acids. More importantly, Tuunanen does not disclose securely and sealingly closing the reservoir tubes. The reservoirs and wand in Tuunanen have no means to sealingly close as is required by the invention so that agitation will not result in loss of liquid sample. The wand in Tuunanen has a handle 6, but this is only for holding the wand and does not act as a sealing mechanism. Therefore this reference would not have indicated the present invention as claimed.

It would not have been obvious to combine Piasio et al with Tuunanen to arrive at the present invention because Piasio et al. teaches away from microstructures and neither reference teaches sealing the reservoir tube. Further, neither reference teaches purifying nucleic acids.

The remaining references of Ji et al, Henco et al., and Lockhart et al. do not suggest the feature of increasing surface area with microstructures.

Ji et al. describes a triplex-mediated capture method for isolation of specific target tract from circular bacterial DNA using a specific oligonucleotide sequence and a solid support such as magnetic beads. The present invention claims the use of a capture assembly that contains a wand and microstructures. The use of this capture assembly does not require use of magnetic field, filter paper, or column packing material (which requires gravitational or pressure forces) as required by Ji's invention. Therefore, Ji et al. would not have motivated one of ordinary skill in the art to arrive at the present invention when combined with Piasio et al. or Tuunanen.

Henco et al. discloses a device that requires preprocessing of the samples outside the device, e.g., precipitation, aggregation or centrifugation. comprising a porous matrix bed in a column that contains silica gel or teflon particles. The process described by Henco et al. for immobilizing, washing and elution of DNA requires gravitational or pressure forces. In the present invention, the sample is processed in the device itself (the reservoir) without the need of centrifugation and does not require gravitational or pressure forces for washing or elution of the DNA. Further, there is no teaching of using a wand with microstructures in this reference either. There is also no teaching of securing and sealing the reservoir tube with the wand in it so that agitation can take place. Because of these deficiencies, Henco et al. would not have motivated one of ordinary skill in the art to arrive at the present invention when combined with Piasio et al, Tuunanen and Ji et al.

Finally, Lockhart et al. fails to describe a method of purification. Lockhart et al. is directed to the synthesis of polymers. Lockhart et al. describes surface-bound, unimolecular, double-stranded DNA relating to the field of polymer synthesis and double-stranded oligonucleotide library screening. Lockhart et al. does not teach devices

and methods for purification of nucleic acids. Lockhart et al. does not include any component such as a wand that is similar to the claimed capture assembly, nor include the microstructure described in the claimed invention. Thus, Lockhart et al. does not make up for the deficiencies of the Ji, et al., Henco, et al., or Piasio, et al.

In conclusion, none of the cited references, whether taken alone or in combination, would have lead one of ordinary skill in the art to the present invention because none of them provide a method for DNA or RNA purification that employs a wand having a sample collection assembly with microstructures. No single invention or combination of inventions cited by the Examiner contains all the features claimed in the present invention in terms of simplicity and adaptability. Further, none of the references provide the required motivation in the form of some statement or suggestion to make their combination as required by 35 U.S.C. §103(a) that would have lead one of ordinary skill in the art to the presently claimed invention, especially since Piasio et al. actually teaches away from the use of microstructures on a wand and interfering with washing steps. Therefore, the rejection under 35 U.S.C. §103(a) is believed overcome.

Reconsideration and allowance are respectfully requested. The Examiner is invited to telephone Applicant's representative at (301) 924-9500 if it would in any way expedite prosecution.

Respectfully submitted,

Date: July 1, 2002 By:

Caroline Nash, Reg. No. 36, 329
Nash & Titus, LLC
3415 Brookeville Rd., Suite 1000
Brookeville, MD 20833

Elizabeth Arwine, Reg. No. 45,867
U.S. Army Medical Research and
Materiel Command,
Attn: MCMR-JA,
Fort Detrick, MD 21702-5012